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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,408	03/12/2001	Mathew F. Ogle	1416.20US01	1108

27367 7590 10/24/2005

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 10/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,408	OGLE ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-28 and 34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11-28 and 34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A response of 8/15/05 presented arguments and did not amend the claims.

Claims examined on the merits are 1-9, 11-28 and 34-43, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-9, 11-28 and 34-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogle et al (5,958,669) in view of Yang et al (5,935,168) for reasons in the previous office actions of 4/15/05, and for reasons herein.

The claims are drawn to tissue containing linkers bonded to tissue and bridge molecules bonded between two or more of the linkers, to a method of crosslinking tissue to prepare the tissue having linkers and bridge molecules, to tissue containing modified sites having bridge molecules bonded to two or more of the modified sites, and to a method of crosslinking tissue to prepare the tissue having modified sites and bridge molecules. In all these embodiments, functional groups of the bridges are required to be generally non-reactive with other bridges.

Ogle et al disclose crosslinking tissue to fix tissue by reacting the tissue with glutaraldehyde.

Yang et al disclose crosslinking tissue with glutaraldehyde, and then reacting with a diamine followed by reacting with additional glutaraldehyde (col 1, line 43 and claims 8-10).

After reacting with glutaraldehyde as disclosed by Ogle et al, it would have been obvious to react with a diamine and then with additional glutaraldehyde as suggested by Yang et al. This will result in the diamine being a linker and the glutaraldehyde being bridge. Additionally, after initially crosslinking with glutaraldehyde some free aldehyde groups will remain that will react with the diamine and result in the glutaraldehyde being a linker and the diamine being a bridge. The aldehyde groups of glutaraldehyde are generally non-reactive with other aldehyde groups of another glutaraldehyde under certain conditions disclosed by Ogle et al that control self-polymerizing. The amine groups of a diamine will not react with amine groups of another diamine. This will result in a bridge not reacting with another bridge.

Response to Arguments

Applicant's arguments filed 8/15/05 have been fully considered but they are not persuasive.

Applicants urge that the statement in the previous office action, that the present claims do not exclude groups of the bridges being reactive with primary nitrogens of tissue, has no bearing on patentability of the claims, and this point has not been argued. However, the response of 3/14/05 at page 8, lines 10-15, argued that glutaraldehyde cannot be a bridge since aldehyde groups of

glutaraldehyde will not only react with diamines, but also will react with any other primary nitrogens in tissue. Therefore, this point was clearly previously argued and the above statement was in response to this argument.

Applicants urge that the previous office action asserts (page 4) that Ogle et al disclose how the self-polymerization of glutaraldehyde can be controlled, but the office action fails to explain how this control of self-polymerization can be used in the context of the present invention to control polymerization of glutaraldehyde. However, the office action cited specific portions of Ogle et al (col 4, lines 1-9, col 6, lines 24-30, and col 7, lines 34-39) of how self-polymerization can be controlled. For example, at col 4, lines 1-9, Ogle et al disclose that spontaneous polymerization of dialdehydes can be controlled by appropriate selection of temperature, pH and/or atmospheric control. If polymers do form, a membrane can be used for size selection. At col 6, lines 24-30, it is disclosed that lowering the concentration of cross-linking compound in the source solution reduces the quantity of undesirable large oligomers, and produces a higher quantity of monomers and small oligomers. Further disclosed (col 7, lines 34-39) is that tissue is removed from the cross-linking solution before the cross-linking solution has had time to develop an inappropriate distribution of cross-linking oligomers. Any of these methods can be used in the context of the present invention to control self-polymerization. In fact, the present specification at page 7, lines 11-16, cites Ogle et al as disclosing a method for reducing the

presence of cross-linker polymers of excessive length, and incorporates Ogle et al by reference. As pointed out in the previous office action, "generally non-reactive" does not exclude the bridge undergoing a small amount of self-polymerization that occurs in Ogle et al when reducing the quantity of large oligomers and obtaining a high quantity of monomers.

Applicants urge that Ogle et al use a membrane to obtain a narrow distribution of a highly reactive glutaraldehyde fraction. However, the present specification (page 7, lines 3-16) contains the same type of disclosure as Ogle et al for using a cross-linking agent that is not too large or too small, and refers to Ogle et al of how to obtain a glutaraldehyde fraction for use in the invention. In view of the present specification, it appears the instant claims are intended to encompass a narrow distribution of a glutaraldehyde fraction as disclosed by Ogle et al.

Applicants urge that there is no motivation to react glutaraldehdye cross-linked tissue of Ogle et al with a diamine and again with glutaraldehyde as disclosed by Yang et al. However, the motivation is to mitigate the propensity for subsequent calcification of such tissues as taught by Yang et al (col 3, lines 1-5).

Applicants urge that the purpose of Yang et al is to increase cross-linking density, and not to make bridges. However, following the teachings of will inherently result in bridges being formed. Note that Yang et al disclose (col 6, lines 25-30) forming glutaraldehyde cross-linkages between free terminal amine groups. Additionally, Ogle

et al indicate that unreacted aldehyde groups can result, and when a diamine is added as suggested by Yang et al, the unreacted aldehyde groups will react the diamine resulting in the diamine being bridge. Certain linkages formed in Ogle et al when following the teachings of Yang et al are "bridge" even through Yang et al does not use the term "bridge".

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-

0926. The fax phone number for the organization where this application or proceeding is assigned is 751-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
10/20/05